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EXAMINER	
ROBINSON, BINTA M	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/788,426	DUMAS ET AL.	
	Examiner	Art Unit	
	Binta M. Robinson	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *12* is/are allowed.

6)☒ Claim(s) *1-11, 13-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

The objection to claim 12 and rejection of claims 16, 17, and 22 for lack of enablement of the diseases are rendered moot in light of applicant's amendment of the claims filed 2/22/07.

(old rejections)

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-11 and 13-30 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making salts of the claimed compounds, does not reasonably provide enablement for making prodrugs of the claimed compounds. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art of medicinal chemistry to use the invention. "The factors to be considered [in making an enablement rejection] have been summarized as a) the quantity of experimentation necessary, b) the amount of direction or guidance presented, c) the presence or absence of working examples, d) the nature of the invention, e) the state of the prior art, f) the relative skill of those in that art, g) the predictability or unpredictability of the art, h) and the breadth of the claims", In re Rainer, 146 USPQ 218 (1965); In re Colianni, 195 USPQ 150, Ex parte Formal, 230 USPQ 546. a) Finding a prodrug is an empirical exercise. Predicting if a certain ester of a claimed alcohol, for example, is in fact a prodrug, that produces the active compound metabolically, in man, at a therapeutic concentration and at a useful rate is filled with experimental uncertainty. Although attempts have been made to predict drug metabolism de

novo, this is still an experimental science. For a compound to be a prodrug, it must meet three tests. It must itself be biologically inactive. It must be metabolized to a second substance in a human at a rate and to an extent to produce that second substance at a physiologically meaningful concentration. Thirdly, that second substance must be clinically effective. Determining whether a particular compound meets these three criteria in a clinical trial setting requires a large quantity of experimentation.

b) The direction concerning the prodrugs is found in lines 17-20, page 20 and lines 1-16, page 21. c) There is no working example of a prodrug of a compound the formula I. d) The nature of the invention is clinical use of compounds and the pharmacokinetic behavior of substances in the human body. e) Wolff (Medicinal Chemistry) summarizes the state of the prodrug art. Wolff, Manfred E. "Burger's Medicinal Chemistry, 5ed, Part I", John Wiley & Sons, 1995, pages 975-977. The table on the left side of page 976 outlines the research program to be undertaken to find a prodrug. The second paragraph in section 10 and the paragraph spanning pages 976-977 indicate the low expectation of success. In that paragraph the difficulties of extrapolating between species are further developed. Since, the prodrug concept is a pharmacokinetic issue, the lack of any standard pharmacokinetic protocol discussed in the last sentence of this paragraph is particularly relevant. Banker (Modern Pharmaceutics) Banker, G.S. et al, "Modern Pharmaceutics, 3ed.", Marcel Dekker, New York, 1996, pages 451 and 596. in the first sentence, third paragraph on page 596 states that "extensive development must be undertaken" to find a prodrug. f) Wolff (Medicinal Chemistry) in the last paragraph on page 975 describes the artisans making Applicants' prodrugs as a collaborative team of synthetic pharmaceutical chemists and metabolism experts. All would have a Ph. D. degree and several

years of industrial experience. g) It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved", and physiological activity is generally considered to be an unpredictable factor. See In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). h) The breadth of the claims includes all of the hundreds of thousands of compounds of formula of claim 1 as well as the presently unknown list of potential prodrug derivatives embraced by claim 1.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim(s) 1-11 and 13-30 in part are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. In claims 1-11 and 13-30 in part, the term "metabolite" is indefinite. A metabolite is not the same chemical species as the compound being claimed, and it is unclear as to what chemical species are being claimed. Appropriate clarification is required.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-11 and 13-15, 18-21, 23-30 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating some tumor growth, some cancers, retinopathy, ischemic retinal-vein-occlusion, age related macular degeneration, rheumatoid

arthritis, psoriasis, dermatitis herpetiformis, erythema multiforme, bullous pemphigoid, subepidermal blister formation, tuberculosis, Helicobacter pylori infection during peptic ulcer disease, Chaga's disease resulting from Trypanosoma cruzi infection, does not provide enablement for preventing any disease in a mammal mediated by the VEGF-induced signal transduction pathway, preventing any disease characterized by abnormal angiogenesis or hyperpermability processes, or treating all of these said diseases, as well as preventing or treating all effects of Shiga-like Toxin resulting from E. Coli infection, effects of enterotoxin A resulting from Staphylococcus infection, meningococcal infection, and infections from Borrelia burgdorferi, Treponema pallidum, cytomegalovirus, influenza virus, Theiler's encephalomyelitis, and the Human (HIV), treating all cancers or all types of tumour growtn, or all hyperproliferative disorders, or treating all diseases regulated by tyrosine kinase or all bolus disorders associated with subepidermal blister formation. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

In In re Wands, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. § 112, first paragraph, have been described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

The nature of the invention

The nature of the invention is the treatment and prevention of hyperproliferative-disorders, all cancers, treating or preventing a disease regulated by tyrosine kinase, treating or prevening a disease mediated by the VEGF-induced signal transduction pathway, treating or preventing a disease in a human mammal characterized by abnormal angiogenesis or hyperpermeability processes, treating or preventing retinopathy, ischemic retinal-vein occlusion, retinopathy of prematurity, age-related macular degeneration; rheumatoid arthritis, psoriasis, a bolos disorder associated with subepidermal blister formation, including bullous pemphigoid, effects of Shiga-like Toxin resulting from E. Coli infection, effects of enterotoxin A resulting from Staphylococcus infection, meningococcal infection, and infections from Borrelia burgdorferi, Treponema pallidum, cytomegalovirus, influenza virus, Theiler's encephalomyelitis, and the Human (HIV), treating all cancers, or all hyperproliferative disorders, or treating all diseases regulated by tyrosine kinase or all bolus disorders associated with subepidermal blister formation.

The state of the prior art and the predictablility or lack thereof in the art

The state of the prior art is that it involves screening in vitro and in vivo to determine which compounds exhibit the desired pharmacological activities (i.e. what compounds can treat which specific disease). There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic or preventive regimen on its face.

The instant claimed invention is highly unpredictable as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instant claimed invention is highly unpredictable since one skilled in the art would recognize that in regards to therapeutic and preventive effects of all diseases, whether or not the disease is effected by the inhibition of raf kinase signaling pathway would make a difference.

The state of the prior art is that cancer therapy remains highly unpredictable. The various types of cancers have different causative agents, involve different cellular mechanisms, and consequently, differ in treatment protocol.

It has been shown that inhibiting the effect of active ras by inhibiting the raf kinase signaling pathway by administration of deactivating antibodies to raf kinase or by co-expression of dominant negative raf kinase or dominant negative MEK, the substrate of raf kinase, leads to the reversion of transformed cells to the normal growth phenotype. See page 1, lines 20-25 of the specification. Similarly, inhibition of raf kinase by antisense olgodeoxynucleotides has been correlated in vitro and in vivo with inhibition of the growth of a variety of human tumor types. See pages 28-20 of the specification. However, because of the complex nature and the multiple growth factors involved in tumor progression, an agent targeting a single pathway may have limited efficacy.

In the absence of a showing of correlation between all the diseases claimed as capable of treatment by the inhibition of raf-kinase pathway, one of skill in the art is unable to fully predict

possible results from the administration of the compound of claim 1 due to the unpredictability of the role of the inhibition of raf kinase pathway and all of the diseases claimed.

The amount of direction or guidance present and the presence or absence of working examples

The only direction and guidance present in the specification is the treatment of the claimed diseases by for the inhibition of raf kinase pathway. There is no correlation between the inhibition of raf kinase pathway with all of the claimed diseases, i.e. the specification fails to provide guidance as to what diseases are mediated by the inhibition of raf kinase pathway.

The breadth of the claims

The breadth of the claims is the treatment of all diseases claimed with the compound of claim 1, the treatment and prevention of hyperproliferative-disorders, all cancers, treating or preventing a disease regulated by tyrosine kinase, treating or prevening a disease mediated by the VEGF-induced signal transduction pathway, treating or preventing a disease in a human mammal characterized by abnormal angiogenesis or hyperpermeability processes, treating or preventing retinopathy, ischemic retinal-vein occlusion, retinopathy of prematurity, age related macular degeneration; rheumatoid arthritis, psoriasis, a bolos disorder associated with subepidermal blister formation, including bullous pemphigoid, effects of Shiga-like Toxin resulting from E. Coli infection, effects of enterotoxin A resulting from Staphylococcus infection, meningococcal infection, and infections from Borrelia burgdorferi, Treponema pallidum, cytomegalovirus, influenza virus, Theiler's encephalomyelitis, and the Human (HIV), treating all cancers, or all hyperproliferative disorders, or treating all diseases regulated by tyrosine kinase or all bolus disorders associated with subepidermal blister formation.

The quantity of experimentation needed

The quantity of experimentation needed is undue experimentation. One of skill in the art would need to determine what diseases out of all diseases would be benefited by the inhibition of raf-1 kinase pathway and would furthermore then have to determine which of the claimed compounds would provide treatment of the disease.

The level of the skill in the art

The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by in vitro and in vivo screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Thus, the specification fails to provide sufficient support of the broad use of the compound of the claim 1 for the treatment of any disease. As a result necessitating one of skill to perform an exhaustive search for which diseases can be treated by what compounds of claim 1 in order to practice the claimed invention.

Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001 , states that " a patent is not a hunting license. It is not a reward for search , but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the Wands factors and In re Fisher (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in

undue experimentation to test which diseases can be treated by the compound encompassed in the instant claims, with no assurance of success.

Claims 1-11 and 13-30 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for using the compounds of formula I with B equal to phenyl, does not reasonably provide enablement for using the compounds of formula I B is napthyl, pyridinyl or quinolinyl optionally substituted as claimed. Compounds made and tested represent the scope of claim 1. The specification does not enable any skilled pharmacologist or physician to use the invention commensurate in scope with these claims. The factors to be considered in making an enablement rejection have been summarized above.

a) Determining if any particular claimed compounds with B is napthyl, pyridinyl or quinolinyl would be active would require synthesis of the substrate and subjecting it to testing with Applicants' raf –1 biochemical assay. Considering the large number of compounds to be made this is a large quantity of experimentation. b) The direction concerning the claimed compounds is found in line pages 93-127 which merely states Applicants' intent to make and use such compounds. c) In the instant case none of the working examples contains any compounds with radical B equal to pyridinyl, napthyl, or quinolinyl. None of these working examples contain a basic or acidic group. d) The nature of the invention is inhibition of raf-1 kinase and treatment of human diseases with Applicants' compounds. This involves physiological activity. The nature of the invention requires an understanding of the raf kinase receptor, the binding activity of small ligands to that receptor, and the ability of those compounds to inhibit this receptor. In view of the unpredictability of receptor binding activity and claimed divergent substituents with varied polarity, size, and polarisability, the skilled physician would indeed

question the inclusion of such diverse rings, commensurate in scope with these claims. Also see the MPEP § 2164.03 for enablement requirements in the structure sensitive arts of pharmacology and medicinal chemistry.

e) The six-membered benzene ring of Applicants' working examples 1-174 on pages 93-127 compounds is non-basic. The pyridine ring, and quinolinyl ring however, of the rejected compounds are strongly basic, basic, and weakly basic respectively. The pyridine and quinolinkyl rings of the rejected compounds are hydrogen bond acceptors. The benzene ring of Applicants' working examples is not. The pyridine ring and the pyrazine ring of the rejected compounds are π-electron deficient. The benzene ring of Applicants' working examples is not. There is no reasonable basis for the assumption that the myriad of compounds embraced the present formula (I) will all share the same biological properties. The diverse claimed fused heteroaryl rings are chemically non-equivalent with each other and with phenyl and napthyl rings and there is no basis in the prior art for assuming in the non-predictable art of pharmacology that structurally dissimilar compounds will have such activity, In re Surrey 151 USPQ 724 (compounds actually tested which demonstrated the asserted psychomotor stimulatory and anti-convulsant properties were those having the 3,4-dichlorophenyl substituent at the 2-position on the thiazolidone nucleus not sufficient for enablement of any heterocyclic radical at the same position). In re Fouche, 169 USPQ 429 at 434 (a Markush group including both aliphatic and heterocyclic members not enabled for the use of those compounds within the claim having heterocyclic moieties.) In re CAVALLITO AND GRAY, 127 USPQ 202 (claims covering several hundred thousand possible compounds, of which only thirty are specifically identified in appellants' application, not enabled unless all of the thirty specific compounds disclosed had

equal hypotensive potency because that fact would strongly indicate that the potency was derived solely from the basic structural formula common to all of them. A wide variation in such potency would suggest that it was due in part to the added substituents and might be eliminated or even reversed by many of the possible substituents which had not been tried.)

f) The artisan using Applicants' invention to treat diseases with the claimed compounds would be a physician with a MD degree and several years of experience. He would be unaware of how to predict a priori how a changing a heterocyclic ring would affect biological activity. In view of the divergent rings with varied basicity, steric hindrance, and polarisability, the skilled physician would indeed question the inclusion of such fused rings, commensurate in scope with these claims. g) Physiological activity, is well-known to be unpredictable, In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) (contrasting mechanical and electrical elements with chemical reactions and physiological activity). See also In re Wright, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); In re Vaeck, 947 F.2d 488, 496, 20 USPQ2d 1438, 1445 (Fed. Cir. 1991). h) The breadth of the claims includes all of millions of compounds of formula (I). Thus, the scope is very broad. The present claims embrace various heterocyclic radicals, which are not art-recognized as equivalent. The specific compounds made are not adequately representative of the compounds embraced by the extensive Markush groups instantly claimed.

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557,1562, 27

USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here. Thus, undue experimentation will be required to practice Applicants' invention.

Response to Applicant's Remarks

The applicant's traverse the lack of enablement, 1st paragraph rejection of the term "prodrug", alleging that the examiner has not provided any evidence to the contrary that the term "prodrug" is not enabled. However, this is not so. As stated in the rejection that has been maintained, determining prodrugs of compounds, is an empirical exercise, that can only be determined by experiment. As stated in the maintained rejection above, Predicting if a certain ester of a claimed alcohol, for example, is in fact a prodrug, that produces the active compound metabolically, in man, at a therapeutic concentration and at a useful rate is filled with experimental uncertainty – and can not be predicted just on the recitation of methods for synthesizing prodrugs in 10 publications as stated on page 28 of the remarks. Applicants mention that esters of appropriate compounds of this invention are well tolerated as prodrugs, however, does give other examples of prodrugs of these compounds. Applicant has not shown that he is in possession of the claimed invention, because he has not shown exemplified prodrugs in the specification with pharmaceutical data that meets the 3 part test for prodrugs: It must itself be biologically inactive. It must be metabolized to a second substance in a human at a rate and to an extent to produce that second substance at a physiologically meaningful concentration. Thirdly, that second substance must be clinically effective. Determining whether a particular compound meets these three criteria in a clinical trial setting requires a large quantity of experimentation. An unreasonable amount of experimentation would be required to determine

the prodrugs of the claimed compounds, including those prodrugs which are esters, and those which are other than esters.

The applicant also traverses the 112, second paragraph rejection of the term "metabolite" pointing to the allowance of the term in other patents. However, other patents can not be used as a basis for examining this patent application. Additionally, it is not clear if metabolites would also encompass prodrugs, which have already been rejected. The metabolites of the compounds are not clearly defined as the applicant asserts, because there is only one example provided, and metabolites, as the applicant states can be any derivative of the claimed compounds produced by metabolism.

Applicants also traverse the rejection of claims 1-11, 13-30 regarding the lack of enablement of the compounds where the radical B is other than phenyl. Applicants allege that the examiner has not submitted any evidence to support the lack of enablement rejection. However, this is not so. The examiner stated on page 10 of the last outstanding office action, that to see if compounds wherein B is equal to napthyl, pyridinyl, or quinolinyl would be active would require a large quantity of experimentation because these compounds would have to be synthesized, and then subjected to Applicant's raf-1 biochemical assay. This experimentation would be undue. Applicant does not synthesize these compounds, nor does the applicant disclose any data regarding the physiological activity of these compounds on the inhibition of raf-1 kinase and the claimed diseases. Additionally, a pyridine ring has different chemical characteristics than a quinolinyl ring or a napthyl ring or phenyl ring, and therefore, there is no reasonable basis that compounds of formula I claimed with B equal to phenyl will share the same same biological properties as compounds of formula I with B equal to quinolinyl, phenyl or napthyl. The

applicant only points to copending applications wherein the compounds of formula I are claimed wherein B is equal to pyridine – and alleges that these compounds are effective Raf –1 kinase inhibitors. The applicant alleges that examples such as example 24, disclosed in the specification of copending application 09640780, illustrate that urea compounds wherein the moiety B is pyridinyl are effective inhibitors of raf and p38. However, these urea compounds are not the compounds of the current invention and differ at the A moiety, wherein in the copending application, the A moiety is isoxazolyl, and in the instant application, A can not be isoxazolyl. Therefore, these compounds in the copending application differ at more than 2 points – at the A and B moieties and are not predictive of the activity of the instant compounds. In copending application 09458014, the compounds that applicants reference also are dissimilar to the instant compounds in that they differ from the instant compounds at the A and B moieties. The A ring in the copending application cannot be any of the A rings in the instant compounds – and the B moiety is pyridinyl and not phenyl. Therefore, are not predictive of the activity of the instant compounds. Additionally, the applicant does not address the efficacy and activity of the claimed compounds when B is other than phenyl or pyridinyl.

Applicant also traverses the 112, first paragraph lack of enablement rejection of the method of treating claims 14, 15, and 23 alleging that the activity, dosages and methods of administrations of these compounds were adequately described and alleging that the examiner provides no evidence to dispute the findings of the publications regarding raf kinase. However, this is not so. The examiner stated in the last outstanding office action in the rejection that because of the complex nature and the multiple growth factors involved in tumor progression, an agent targeting a single pathway may have limited efficacy. Furthermore, the rejection also

noted that the applicant failed to demonstrate a correlation between the inhibition of raf kinase pathway with all treatment of the claimed diseases. Additionally, it was noted that the state of the prior art is that cancer therapy remains highly unpredictable. The various types of cancers and hyperproliferative disorders have different causative agents, involve different cellular mechanisms, and consequently, differ in treatment protocol. Therefore, the applicant has not shown how the current compounds can treat all cancers or hyperproliferative disorders. It also is not established in the art to prevent hyperproliferative disorders or preventing any of the disease in claim 15, claims 18-21, 23.

Claim 12 is allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Binta M. Robinson whose telephone number is (571) 272-0692. The examiner can normally be reached on M-F (9:30-6:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Janet Andres can be reached on 571-272-0867.

A facsimile center has been established. The hours of operation are Monday through Friday, 8:45 AM to 4:45 PM. The telecopier numbers for accessing the facsimile machine are (703)308-4242, (703)305-3592, and (703)305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571)-272-1600.

BMR
November 13, 2007

JANET L. ANDRES
SUPERVISORY PATENT EXAMINER